PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To: TERESA STANEK REA
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PCT

WRITTEN OPINION

(PCT Rule 66)

Date of Mailing *(day/month/year)*	24 NOV 2003
Applicant's or agent's file reference: 033388-532	REPLY DUE within TWO months from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US03/00377	08 JANUARY 2003	09 JANUARY 2002

International Patent Classification (IPC) or both national classification and IPC
IPC(7): A 61K 9/127 and US Cl.: 424/450; 264/4.1, 4.3

Applicant
ELAN PHARMACEUTICALS, INC.

1. This written opinion is the first (first, etc.) drawn by this International Preliminary Examining Authority.

2. This opinion contains indications relating to the following items:

- I [X] Basis of the opinion
- II [ ] Priority
- III [ ] Non-establishment of opinion with regard to novelty, inventive step or industrial applicability
- IV [ ] Lack of unity of invention
- V [X] Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI [ ] Certain documents cited
- VII [ ] Certain defects in the international application
- VIII [ ] Certain observations on the international application

3. The applicant is hereby invited to reply to this opinion.

When? See the time limit indicated above. ~~The applicant may, before the expiration of that time limit, request this Authority to grant an extension., see Rule 66.2(d).~~

How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

Also For an additional opportunity to submit amendments, see Rule 66.4.
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 *bis*.
For an informal communication with the examiner, see Rule 66.6.

If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: 09 MAY 2004

Name and mailing address of the IPEA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231	Authorized officer Valerie Ball-Harris for GOLLAMUDI S KISHORE
Facsimile No. (703) 305-3230	Telephone No. (703) 308-1235

Form PCT/IPEA/408 (cover sheet) (July 1998)★

WRITTEN OPINION

International application No.
PCT/US03/00377

I. Basis of the opinion

1. With regard to the elements of the international application:*

[X] the international application as originally filed

[X] the description:
pages 1-53 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the claims:
pages 54-79 , as originally filed
pages NONE , as amended (together with any statement) under Article 19
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the drawings:
pages 1-18 , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

[X] the sequence listing part of the description:
pages NONE , as originally filed
pages NONE , filed with the demand
pages NONE , filed with the letter of _____

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.
These elements were available or furnished to this Authority in the following language _____ which is:

[ ] the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).

[ ] the language of publication of the international application (under Rule 48.3(b)).

[ ] the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the written opinion was drawn on the basis of the sequence listing:

[ ] contained in the international application in printed form.

[ ] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority in written form.

[ ] furnished subsequently to this Authority in computer readable form.

[ ] The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

[ ] The statement that the information recorded in computer readable form is identical to the writen sequence listing has been furnished.

4. [X] The amendments have resulted in the cancellation of:

[X] the description, pages NONE

[X] the claims, Nos. NONE

[X] the drawings, sheets/~~fig~~ NONE

5. [ ] This opinion has been drawn as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

** Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*

WRITTEN OPINION

International application No.
PCT/US03/00377

V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. statement

Novelty (N)	Claims	1-106	YES
	Claims	NONE	NO
Inventive Step (IS)	Claims	NONE	YES
	Claims	1-106	NO
Industrial Applicability (IA)	Claims	1-106	YES
	Claims	NONE	NO

2. citations and explanations

Claims 1-7, 9-12, 18-51 and 53-106 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al (US 5,741,513).

GHYCZY et al disclose a method of preparation of liposomes. The method involves dissolving the phospholipid concentrate in ethanol and adding an aqueous medium to prepare a gel and then adding more aqueous medium to prepare the liposomes (col. 3, line 24 through col. 5, line 56 and Examples. What is lacking in GHYCZY et al is the claimed amount of the acidic phospholipid. However, in the absence of showing unexpected results, it is deemed obvious to manipulate the amounts of the acidic phospholipids taught by GHYCZY et al with the expectation of obtaining the best possible product.

Claims 8 and 52 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above, further in view of IGA et al (US 4,877,561).

The teachings of GHYCZY et al have been discussed above. what is lacking in GHYCZY et al is the teaching of the use of acetone as the solvent.

IGA et al while disclosing a liposome gel formulation containing a variety of drugs teach that for the formation of liposome gels, organic solvents such as alcohols and acetone can be used (abstract, col. 1, line 63 through col. 3, line 34).

The use of acetone instead of alcohol taught by GHYCZY et al would have been obvious to one of ordinary skill in the art since the reference of IGA et al shows that acetone could be used instead of alcohol.

Claims 13-17 lack an inventive step under PCT Article 33(3) as being obvious over GHYCZY et al cited above, further in view of KIRPOTIN et al (US 5,980,935).
(Continued on Supplemental Sheet.)

Supplemental Box
(To be used when the space in any of the preceding boxes is not sufficient)

Continuation of: Boxes I - VIII

TIME LIMIT:

The time limit set for response to a Written Opinion may not be extended. 37 CFR 1.484(d). Any response received after the expiration of the time limit set in the Written Opinion will not be considered in preparing the International Preliminary Examination Report.

V. 2. REASONED STATEMENTS - CITATIONS AND EXPLANATIONS (Continued):

The teachings of GHYCZY et al have been discussed above. what is lacking in GHYCZY et al are the teachings of nucleic acids and plasmids as the active agents. The use of nucleic acids and plasmids as the active agents however, would have been obvious to one of ordinary skill in the art since the reference of KIRPOTIN et al shows that these agents are routinely incorporated in liposomes for transfection purposes (note the abstract and Examples).

Claims 1-106 meet the criteria set out in PCT Article 33(2)and(4), because the prior art does not specifically teach a method of formation of liposomes using instant amounts of phospholipids and since the invention finds its utility in the preparation of liposomes and the delivery of a variety of active agents.

---------- NEW CITATIONS ----------

US 4,877,561 A (IGA et al) 31 October 1989, see abstract, col. 1, line 63 through col. 3, line 34.

US 5,980,935 A (KIRPOTIN et al) 09 November 1999, see abstract and Examples.